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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KIM, TAEYOON	
ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/521,071	LIM, SAI KIANG	
	Examiner	Art Unit	
	Taeyoon Kim	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-26* is/are pending in the application.

4a) Of the above claim(s) *15-18 and 23-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/25/05; 2/1/06; 12/2/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 15-26 are pending.

Election/Restrictions

Applicant's election with traverse of Group II (claims 19-22) in the reply filed on Oct. 2, 2006 is acknowledged. The traversal is on the ground(s) that 1) there is a special technical feature present in the claimed invention, and 2) there is no serious search burden. This is not found persuasive. The groups of invention disclosed in the current application are composed of multiple methods and compositions. PCT Rule 13.2 does not provide for multiple compositions or multiple methods of use within a single application. Thus, the first appearing composition (Group I) is combined with a corresponding first method of use (Group IV) and the additional composition and method claims each constitute a separate group. There is a common technical feature between Group I and Group IV inventions, which is "hemangioblast". Since the reference (Lacaud et al.) teaches "hemangioblast", this technical feature is no "special". Applicant argues that there are four properties of "hemangioblast" which is not disclosed in the reference. However, these four properties are not commonly claimed in both Group I and IV. In claim 24, hemangioblast cells are referred to claim 17. This is not considered as a limitation to the hemangioblast, rather it is a mere reference to the cells. Therefore, Group IV does not contain the four properties that Applicant argued about.

Applicant alleges that there would be no burden on the examiner in examining all of the claims at once, relying on M.P.E.P. §802.02. Chapter 800, however, is limited to a

discussion of the subject of restriction and double patenting under Title 35 of the United States Code and Title 37 of the Code of Federal Regulations as it relates to national applications filed under 35 U.S.C. 111(a). The discussion of unity of invention under the Patent Cooperation Treaty Articles and Rules as it is applied as an International Searching Authority, International Preliminary Examining Authority, and in applications entering the National Stage under 35 U.S.C. 371 as a Designated or Elected Office in the U.S. Patent and Trademark Office is covered in M.P.E.P. §1850 and is dictated by PCT Rules 13.1 and 13.2. See M.P.E.P. §801. Burden is not a consideration in a finding of lack of inventive unity; rather, according to M.P.E.P. §1850, the only consideration is whether the inventions share a special technical feature.

Therefore, the requirement is still deemed proper and is therefore made **FINAL**.

Claims 27 and 28 have been cancelled. Claims 15-18 and 23-26 have been withdrawn from consideration as being drawn to non-elected subject matter. Claims 19-22 have been considered on the merits.

Information Disclosure Statement

The information disclosure statement filed on Dec. 12, 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Objections

Claim 20 is objected to because of the following informalities: There is an apparent typo in the claim. In the second line of the claim, "...the step of..." appears to be "... a step of ...". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase in 5th line of claim 19 is not clear what the subject matter it points out. There are apparently three populations of cells disclosed in this phrase: fibroblastic cells, round cells, and ring-like cells. It is not clear whether these three populations are the same cell populations; round cells are the same as ring-like cells; or each belongs to different cell population. In addition, "...round cells having ring-like cells..." is not clear whether these two "round" cells and "ring-like" cells are the same cells.

It is not clear what the subject matter the term "ring-like cells" are pointing out.

It is not clear what the subject matter the term "delayed" in the second line of claim 19 points out. It is not clearly defined what "delayed" means in the specification.

It is not clear what the subject matter the term "integrity" in claim 20 points out.

It is not clear what the subject matter the term "selected cells" in the second line of claim 22 points out. The selected cells could be cells in selected colonies of adherent fibroblastic cells with loosely attached rapidly dividing round cells having ring-like cells or cells selected from the group consisting of a delayed mammalian blastocyst, an early post-implantation embryo, an embryonic stem cell-derived embryoid body, or bone marrow tissue.

Claims 19-22 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the final step of selecting and growing a certain cell. The current invention is a method of preparing a mammalian cell line. However, there is no step claimed in the instant claims which cells are selected for the cell line after the step (iii) of testing cells for ability to differentiate into both endothelial and hematopoietic cells. It appears that the current application is drawn to the method to generate a cell line that possesses a capability to differentiate into both endothelial and hematopoietic cells. Therefore, it is critical to have a final step of selecting and growing a cell population having the above ability after the step (iii) of testing cells.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirements. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant claims a method to generate a mammalian cell line having an ability to differentiate into both endothelial and hematopoietic cells. Cells with such ability are known as "hemangioblast" as disclosed in the current application and they have long been under debate and controversy. The cells have been known as "hypothetical" as disclosed by Choi et al. (1998, IDS reference C3) and Keller (2001). In addition, a review article by Mikkola et al. (2002) states that the ultimate proof for the existence of a hemangioblast is lacking, although evidence (such as Choi et al. supra) has been gained to demonstrate the existence of precursor cells that are able to give rise to at least restricted hematopoietic and endothelial progeny (see p.9, left column). With such a uncertainty of "hemangioblast" cells and lack of proof of their presence, it is difficult to expect that a person of ordinary skill in the art at the time of invention would carry out the method of the current invention with success. Furthermore, the step (iii) of testing cells for ability to differentiate into both endothelial and hematopoietic cells is not fully and clearly described in the specification to enable a person of ordinary skill in the art to make "hemangioblast" cell lines. For example, in the specification (p.14, lines 4-6), applicant discloses that the applicant's hemangioblast cells do not display markers such as CD34, PECAM-1, Flk-1, Tie-2, Sca-1, Thy-1 or P-selection. To the contrary, these

markers are disclosed as typical endothelial and hematopoietic markers (p.14, lines 20-23). This discrepancy raises a question how to test the selected cells for ability to differentiate into endothelial and hematopoietic cells. Therefore, a person of ordinary skill in the art would not have a reasonable expectation and predictability of success to isolate "hemangioblast" cells by the method of the current application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 19 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Choi et al. (1998; IDS C3).

Claims 19 and 22 are drawn to a method of preparing a mammalian cell line having steps of (i) culturing delayed mammalian blastocyst or embryonic stem cell-derived embryoid body on a feeder layer, (ii) selecting colonies of adherent cells with round cells having ring-like cells, (iii) testing cells in the selected colonies for ability to differentiate into both endothelial and hematopoietic cells (claim 19); a limitation to the method further comprising maintaining cells on a gelatinized feeder-free layer (claim 22).

Choi et al. teach a method of culturing and preparing hemangioblast cells, the common precursor of the hematopoietic and endothelial lineage using embryonic stem

cell-derived embryoid body from mouse or delayed blastocysts (7 dpc blast cells) by culturing on STO feeder cells (claim 19) or on gelatinized flasks (claim 22), selecting adherent cells and round hematopoietic cells from blast colony, and testing the expression of markers for endothelial and hematopoietic cells (see Abstract, Materials and Methods, Figs. 1 and 2). Choi et al. also teach that blast colonies are transferred to matrigel (a gelatinous protein mixture) -coated wells, which is a feeder-free layer (see Cell Culture p.726).

Thus, the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 19, 20, 21 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Choi et al. (supra) in view of Shi et al. (1998) in further view of Moore (2002).

Claims 19, 20, 21 and 22 are drawn to a method of preparing a mammalian cell line having steps of (i) culturing bone marrow on a feeder layer, (ii) selecting colonies of adherent cells with round cells having ring-like cells, (iii) testing cells in the selected colonies for ability to differentiate into both endothelial and hematopoietic cells (claim 19); a limitation to the cell source of the method of claim 19 being bone marrow tissue

and the method further comprising a step of harvesting bone marrow tissue prior to the step of culturing (claim 20); a limitation to the cell source being human (claim 21); a limitation to the method further comprising maintaining cells on a gelatinized feeder-free layer (claim 22).

Choi et al. teach a method of generating a mammalian cell line using the steps of claim 19 and the limitations to claim 22 (see above).

Choi et al. do not teach the source of cells being bone marrow tissue.

Shi et al. teach the presence of a common precursor cells for both endothelial and hematopoietic cells from human bone marrow. Cells with endothelial morphology were identified from a transplanted bone marrow graft (see Abstract and Materials and Methods).

It would therefore have been obvious for the person of ordinary skill in the art at the time the invention was made to use bone marrow tissue of Shi et al. in the method of Choi et al. to generate a cell line having an ability to differentiate into both endothelial and hematopoietic cells.

The skilled artisan would have been motivated to make such a modification because the use of cell lines for transplantation using bone marrow allows autologous transplantation as described by Moore (2002), unlike embryonic stem cell derived cell line (see p.315, middle column).

The person of ordinary skill in the art would have had a reasonable expectation of success in obtaining a cell line having ability to differentiate into both hematopoietic and endothelial cells from bone marrow since it has been disclosed that there are cells

in bone marrow having such a property according to Shi et al. (supra) as well as Moore (supra).

Although Choi et al. in view of Shi et al. do not teach a step of harvesting bone marrow tissue in clumps prior to the step of culturing, it is obvious for a person of ordinary skill in the art to use bone marrow to generate a cell line having an ability of differentiation into both endothelial and hematopoietic cells to harvest bone marrow tissue for culturing such a cell population.

Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill at the time the invention was made.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 19-22 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 6-11 of copending Application No. 10/618,540. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

No claims are allowed. No claims are free of art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taeyoon Kim whose telephone number is 571-272-9041. The examiner can normally be reached on 8:00 am - 4:30 pm ET (Mon-Fri).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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